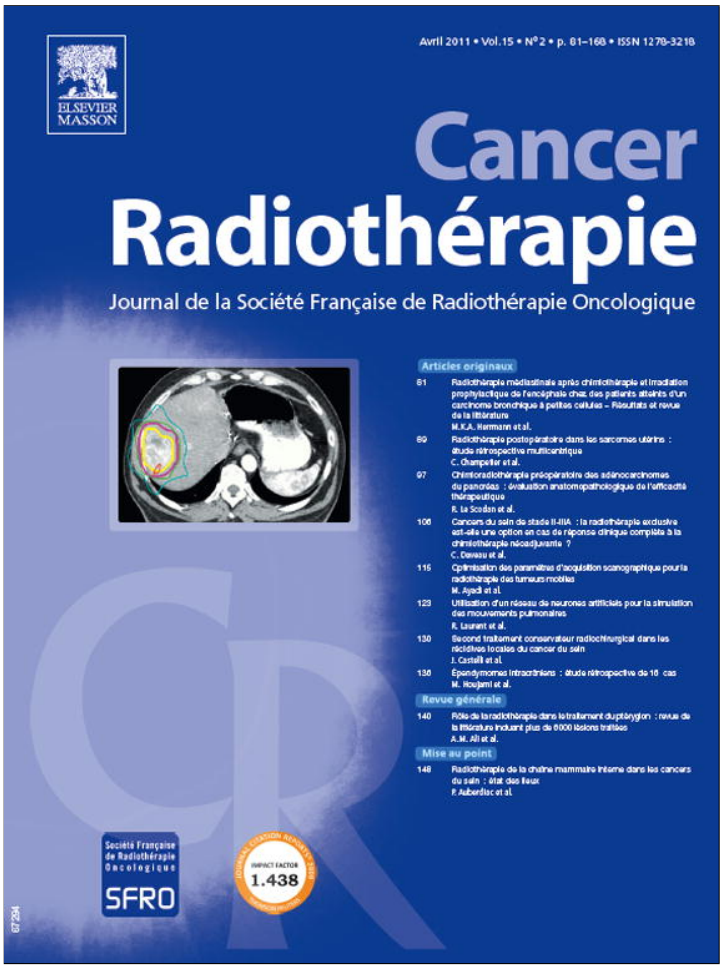

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General review

The role of radiotherapy in the treatment of pterygium: A review of the literature including more than 6000 treated lesions

Rôle de la radiothérapie dans le traitement du ptérygion : revue de la littérature incluant plus de 6 000 lésions traitées

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ABSTRACT

Pterygium is a benign conjunctival neoformation usually treated by surgical excision, but recurrences may affect 30% to 89% of cases, so that adjunctive therapies like conjunctival autografting, antimitotic drugs and beta-irradiation (β-irradiation) are often used to improve the rate of local control. Our essay has reviewed relevant studies addressing the role of postoperative irradiation in the treatment of pterygium in the last 30 years through an Internet-based search and hand search in libraries. Sixteen studies on β-irradiation and one on soft X-ray irradiation were accessible. They covered more than 6000 lesions treated by surgical excision and postoperative β-irradiation using strontium-90 (^{90}Sr) applicators at doses varying from 10 to 60 Gy/1–6 fractions/1–6 weeks starting within 3 days postoperatively. The rates of local recurrence were in general lower than 15% and major complications such as scleral thinning, ulceration, infections, or radiation-induced cataract were rarely encountered. Early postoperative β-irradiation at a dose of 30 Gy/three fractions/2–3 weeks starting within 24 h from surgical excision is an effective and safe procedure with local control rates comparable to chemotherapeutic agents and conjunctival autografting and superior to simple excision alone.

Mots clés :
Ptérygion
Chirurgie
Rayon bêta
Strontium-90
Contrôle local

RÉSUMÉ

Le ptérygion est une tumeur bénigne d'origine conjonctivale. Son traitement est avant tout chirurgical, mais l'exérèse seule est grevée de près de 30 à 89 % de récidives, c'est pourquoi des traitements adjuvants comme l'autogreffe conjonctivale, les substances cytotoxiques, l'irradiation postopératoire au moyen de rayons bêta sont largement utilisées pour réduire ce risque de récidive. Nous avons cherché sur Internet et aussi dans les bibliothèques des études concernant le rôle de la radiothérapie postopératoire dans le traitement de ces lésions pendant les 30 dernières années. Seize études sur le traitement postopératoire à l'aide d'un émetteur bêta (strontium-90) et une seule étude sur les rayons X sont accessibles. Ces études ont inclus plus de 6000 lésions traitées au moyen de l'exérèse chirurgical suivie par une irradiation aux doses de 10 à 60 Gy en une à six séances sur une à six semaines débutées dans les trois jours postopératoires. Les taux de rechute ont globalement été inférieurs à 15 % et les effets secondaires majeurs comme l'atrophie de la sclère, l'ulcération, des infections et la cataracte ont rarement été reportées. Cette revue permet de conclure que l'irradiation postopératoire précoce (notamment l'irradiation bêta), à une dose de 30 Gy en trois fractions et deux à trois semaines, débutée dans les 24 heures suivant l'acte chirurgical, est un traitement efficace et sans effets secondaires majeurs, assurant un taux de contrôle local comparable à celui obtenu par les injections locales de substances cytotoxiques ou par l'autogreffe conjonctivale, et significativement supérieur à celui obtenu par l'exérèse chirurgicale seule.

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1. Introduction

Pterygium is a common conjunctival disorder of unknown etiology [37,43]. It typically develops between the ages of 20 to 50 especially in tropical and subtropical areas and characterized by fibrovascular reaction, chronic inflammatory cells infiltration, angiogenesis, fibroblastic proliferation and invasion [13,21,31,77]. Some studies have indicated that excessive production of extracellular matrix is implicated in its pathogenesis [9,37]. More recently, positive immunostaining for fibroangiogenic growth factors in pterygium has suggested their interactions in cellular proliferation, inflammatory reaction, remodeling of extracellular matrix and angiogenesis of pterygium [8,41]. Also, the demonstration of higher counts of circulating CD34+ and c-kit+ bone marrow derived progenitor cells in correlation with higher levels of systemic and local cytokines and stronger expression of progenitor cell markers such as CD34, c-kit, vascular endothelial growth factor (VEGF1 and VEGR2) in pterygial tissues, especially recurrent ones, than in normal conjunctiva suggested that these progenitor cells are involved in its pathogenesis and environmental factors such as UV, heat and wind might cause chronic inflammation and sublethal hypoxia that triggers the migration of these cells, which can differentiate into mature endothelial cells, to the limbus [43,63]. Anti-apoptotic mechanisms have also been suggested in its pathogenesis, and recent data demonstrated expression of cyclooxygenase-2 (COX-2) and anti-apoptotic protein, survivin, in primary pterygia [19,52]. Such information can provide a base towards the development of novel therapeutic strategies that involve the use of COX-2 and survivin inhibitors [52].

The main treatment of pterygium is surgery [45,49]. Although excision of pterygium with bare sclera technique is the quickest method with the least surgical intervention but it is by far the least satisfactory method with respect to recurrence rate, so that, adjuvant therapy such as conjunctival autografting (CAG), cytotoxic agents like mitomycin C (MMC) and β-irradiation is needed for prevention of recurrences [32,33,35,48].

Although CAG is considered safe and effective procedure with infrequent complications such as epithelial inclusion cysts, corneoscleral dellen, graft oedema, it needs surgical expertise, technical ability and more time to secure the graft with sutures [36,69,72]. However, using fibrin glue instead of sutures was found to shorten the operative time, minimize postoperative discomfort and improve local control [26,36]. Recurrence rates reported with CAG ranged from 5.4 to 39% for primary [2,4,18,45,46,72] and from 5.3 to 33.3% for advanced and recurrent pterygia [2,38,45,72].

Including limbal stem cells in the conjunctival autograft (LCAG) is suggested to act as a barrier to conjunctival cells migrating onto the corneal surface and help preventing recurrence [7]. Some authors reported that LCAG is more effective than CAG with recurrence rates ranged from 1.9 to 7% for primary and up to 14.6% for recurrent lesions [1,2,23,30,39,54,79]. However, it is technically more demanding and time-consuming to perform [7].

Using MMC in treatment of pterygium dates back to 1963 [18]. Some studies reported that low dose topical MMC (0.2 mg/ml twice daily for 5 days to three times daily for 1 week) after excision of pterygium has been as effective as CAG with comparable recurrence rates varied between 3.7 and 38% while others found it was associated with even lower recurrence rate to that achievable with CAG (9.4% versus 24.9%, respectively) [18,46,49]. In view of the various complications reported with postoperative topical MMC such as secondary glaucoma, iritis, cataract, scleral necrosis, scleritis and perforation, a single intraoperative instillation of MMC at concentrations from 0.02% for 3–5 min to 0.04% for 3 min has been considered safe and effective alternative to postoperative MMC as it had been found associated with recurrence rates from 4.08 to 15.9% compared to 29.27–75% for excision alone in primary pterygia and recurrent ones, along with very low rates of side effects such as superficial punctate keratitis, limbal avascularity, superficial scleral melting, scleral dellen and conjunctival cysts [1,6,7,16,22,24,42,50,51,60,65,79].

Utilization of β-irradiation in postoperative treatment of pterygium has a long history being convenient and practical method in inhibiting the repopulation of endothelial cells. It is characterized by minimal tissue penetration and absence of unwanted gamma rays [29,40,53,58,77]. Early studies reported success rates up to 90% with bare sclera excision and postoperative β-irradiation, but others reported it might lead to iatrogenic ocular diseases [20,71]. Few studies have compared between postoperative β-irradiation and MMC and even fewer those compared between β-irradiation and CAG. While some reported lower recurrence rates in favour of intraoperative and postoperative MMC for primary pterygium, others reported better results with β-irradiation compared with postoperative MMC in primary and recurrent pterygia and better, yet marginal, outcome of β-irradiation over CAG in primary pterygia [6,17,21,68]. Our review of literature aims at evaluating the role of postoperative irradiation in reducing the recurrence rate of pterygium and the complications associated with it.

2. Method of review

References enrolled in our review were collected through an Internet-based survey using the PubMed® data searching for English language publications on pterygium and irradiation as well as a hand research in libraries. We have focused on studies reporting on the results of treatment of pterygium whether primary or recurrent by both surgical excision and postoperative ionizing irradiation. Studies on other modalities of treatments and those having incomplete information from published data were not focused on. The study to be relevant to our review had to report on the impact of such a combined treatment on the local control and/or recurrence rates as well as the side effects. We were able to access to 17 studies that composed the bulk of our review. These studies included a total number of more than 6000 treated lesions.

3. Treatment

Treatment of pterygium with β-irradiation using 90Sr applicator is a mould brachytherapy. 90Sr is a nuclear reactor fission product of uranium-235. Its half-life is 29.12 years and decays to yttrium-90 [59]. The applicators consist of silver cups containing the radioisotopes incorporated onto them with thin metallic covering to remove low energy β-particles. Plane sources are typically about 10–12 mm while concave ones from 9 to 23 mm in diameter. The applicator is put manually in contact with the surgical bed and the dose is delivered to the surface. The maximum energy of β-particles emitted from 90Sr is estimated at 0.546 Mev while those from yettrium-90 at 2.27 Mev [53]. The depth dose was found to be 20% at 2 mm, and almost 0% at 5 mm under the surface [10,27,34].

4. Results

4.1. Randomized studies

Prospective randomized trials on treatment of pterygium with surgery and postoperative irradiation are scarce [33,35]. Jürgenliemk-Schulz et al. conducted a prospective, randomized, multicenter, double-blind study included 96 pterygia (Table 1). They analyzed the results of 86 pterygia excised by bare sclera technique followed either by β-irradiation using 90Sr applicator at a dose rate between 200 and 250 cGy/min (44 eyes) or sham radiotherapy using non 90Sr containing applicator (42 eyes). Recur-

Table 1
Summary of the studies on treatment with surgery and postoperative beta irradiation.

Authors	Number of lesions	Dose schedule	Timing postoperative	Follow up	Rate of local control	Late side effects
Jürgenliemk-Schulz et al. [35]	86 (All primary) Surgery and radiotherapy: 51% Surgery only: 49%	25 Gy (single fraction)	Within 24 h	Mean: 18 months	Crude control rate for surgery/radiation: 93.2% vs. 33.3% for surgery alone ($p = 0.004$)	No serious complications.
Nakamatsu et al. [55]	73 pterygia All primary	Group A: 30 Gy/3 fraction/15 days: 56% Group B: 40 Gy/4 fraction/22 days: 44%	Started within 3 days	Median 2 years	2 year local control Rate: 87 and 70% for group A and B respectively	No serious side effects
De Keizer [21]	57 pterygia Primary: 72% Recurrent: 28%	27 or 30 Gy/3 fractions Dose/fraction: 9–10 Gy	At 24 h, 1 week and 2 weeks	6 month–7 years	Recurrence rate: Primary: 0% Recurrent: 12.5%	No scleral melting No glaucoma No cataract
Isohashi et al. [33]	1253 pterygia Primary: 87.95% Recurrent after surgery alone: 9.18% Recurrent after surgery and irradiation: 2.87%	30 Gy/3 fractions/3 weeks: 70.23% 35 Gy/3 fractions/3 weeks with the first fraction 15 at Gy (for lesions treated >48 h after surgery): 29.77%	≤48 h: 57.14% >48 hours: 29.77% Within 2 h: 13.09%	Median 45 months	At 5 years: 90%	No major complications like scleral ulcers, scleromalacia, or scleral necrosis
Paryani et al. [62]	825 primary and recurrent	60 Gy/6 fractions/6 weeks	Within 24 h	Median >8 years	Recurrences: 1.7%	No cataract, or corneal ulcerations
Viani GA et al. [75]	737 pterygia Primary: 87% Recurrent: 13%	35 Gy/7 fractions/10–15 days for irradiation given <48 h postoperatively. 35 Gy/5 fractions/10–15 days for irradiation given >48 h postoperatively.	Range: 1–120 h	Median 60 months	5 and 10 years local control probability: 90 and 88%, respectively.	Visual disturbance (4.2%), congestion: 2.5% Scleromalacia: 1.2% adhesion of eye lids, scleral ulcer: 1.08% for each cataract: 0.8%, and ulceration: 0.5%

Nishimura et al. [57]	490 pterygia Primary: 92.25% Recurrent after Surgery: 3.47% Recurrent after surgery and radiotherapy: 4.28%	38–42 Gy/4–5 fractions/ 22–29 days: (75%). 31.1–37.9 Gy/4–5 fractions/22–29 days: (20.2%) 7.4–28.7 Gy/1–3 fractions/1–22 days: (2.8%) 42.4–49.9 Gy/4–5 fractions/29–43 days:(2%)	1 day: (30.41%) 2 days: (14.49%) 3 days: (32.24%) 6–9 days: (15.51%) 10–86 days: (7.35%)	Median 61 months	For all: 88% and 86% at 5 and 10 years At 10 years: 91%, 94%, 88%, 73% and 65% (for those treated at 1,2, 3, 6–9 and 10–86 days after surgery	Scleral thinning 0.8%, adhesive scar at the eyelid: 0.6% Ischemic necrosis of sclera, infectious scleral ulcer and cataract: 0.2% for each
Fukushima et al. [27]	393 pterygia Primary: 88.55% Recurrent: 11.45%	30 Gy/3 fractions/3 weeks for treatment started <48 h. 35 Gy/3 fractions/3 weeks for treatment started >48 h (number not specified in both)	Within 48 h or longer than 48 h (number not specified in both)	Median 17 months	Overall rate at 1 and 3 years: 93.7% and 85.3%, respectively	No serious side effects.
Wilder et al. [77]	338 pterygia Primary: 84% Recurrent: 16%	3 weekly 8 Gy fraction: 94.97% 2 weekly 8 Gy fraction or single fraction at 8 Gy: 4.14% Single fraction at 10 and 18 Gy: 0.59 and 0.29%	1–8 h: 88.76% 16–24 h: 11.24%	Median 2 years	The crude rate: 88%. At 5 years: 84% (overall rate)	Telangectasia of sclera: 6cases. Granuloma and cataract (3 cases for each). Scleral atrophy: 2 cases.
Wesberry et al. [76]	171 pterygia	20 Gy single fraction	Immediately after surgery	Up to 17 years	Incidence of recurrence: 8%	Minor complications: 3% and scleral thinning: 0.5%

Table 1 (*Continued*)

Authors	Number of lesions	Dose schedule	Timing postoperative	Follow up	Rate of local control	Late side effects
Beyer [11]	146 pterygia (135 evaluable)	30 Gy once: 92.5% 30 Gy/2–3 fractions: 2.8% 40 Gy/2 fractions: 3.3% 45 Gy/3 fractions: 1.4%	Immediately after surgery: 55% Within 24 h: 27.3% and from 2–21 days: 16.4% Unknown: 1.3%	Median 13 months	Actuarial freedom from relapse: 87% Recurrences in single dose: 9.4%. Recurrences in fractionated dose: 12.5%	No serious complications No new cataract
Monteiro-Grillo et al. [53]	100 pterygia Primary (group 1): 37% Recurrent (group 2): 63%	6 weekly of 10 Gy fractions: 80%. 30 Gy/3 fractions every other day: 17% 20 Gy single fraction: 3%	<2 h: 72% 24 h: 18% Mean time of 48 h: 10%	Median 49 months	5 years local control probability: 83 .5%, 94% and 76. 9% for all cases, group 1 and 2 ($p = 0.04$)	No late complications No new cataract

rence was defined as postoperative regrowth of fibrovascular tissue crossing the corneoscleral limbus. The crude recurrence rate was 6.8% versus 66.7% in favor of β-irradiation and most of recurrences developed within 1 year after treatment. Photophobia and irritation appeared in both groups with no significant differences, few cases of postoperative granuloma in the surgery only arm but no severe complications had been noticed [35].

Nakamatsu et al. analyzed the outcome of 73 pterygia excised with bare sclera technique followed by β-irradiation (Table 1). No significant difference in local control was noted between lesions received 30 Gy/three fractions/15 days and those received 40 Gy/four fractions/22 days when radiotherapy started within 3 days after surgery [55].

De Keizer compared between surgical excision and superficial free conjunctival autograft FCG versus excision and postoperative 90Sr β-irradiation (Table 1). While 6.4% of primary lesions treated with FAG recurred, no recurrences developed with β-irradiation. For recurrent lesions, both modalities showed equal results with recurrence rate at 12.5% for each. No serious complications with β-irradiation were noted, and in FAG, granuloma, moved graft, glaucoma and foreign body reaction were reported [21].

4.2. Retrospective studies

Isohashi et al. analyzed the results of 1253 pterygia treated by excision and postoperative β-irradiation (Table 1). Recurrences affected 7.7% of cases. The multivariate analysis gave a significantly lower rate in males, patients younger than 40 years, patients with prior radiotherapy and patients who underwent radiotherapy immediately after surgery versus more than 2 h after surgery with p values of 0.013, <0.001, 0.013 and 0.014, respectively. Temporary side effects e.g. moderate conjunctivitis, local pain, visual disturbance and photophobia developed in 15.2% of cases [33].

Pinkerton reported a recurrence rate at 6% after treatment of 975 pterygia with simple wide excision and immediate postoperative β-irradiation at a maximum dose of 30 Gy [64].

Paryani et al. in a study on 825 pterygia treated by resection and postoperative β-irradiation reported a recurrence rate at 1.7%, most of them developed in the first year (Table 1). Patients who had prior therapy were more vulnerable for other recurrences. No major complications appeared [62].

Viani et al. after excision and postoperative β-irradiation of 737 lesions found a recurrence rate at 9.9% (Table 1). Eighty percent of recurrences developed within 3 years after treatment. For the primary lesions without previous treatment, the recurrence rate was 6% at 5 years. Local control rates were significantly lower with large, recurrent lesions, timing postoperatively >48 h, total doses <35 Gy, and in patients <65 years with p-values of 0.02, <0.0001, 0.001, 0.001 and 0.0001, respectively [75].

Nishimura et al. studied 490 pterygia treated by resection and postoperative β-irradiation (Table 1). Recurrences developed in 11.8%. The median time of recurrences was 10 months in the majority of cases. The local control probability was significantly better for pterygia irradiated within 3 days versus those irradiated from 6 to 9 days postoperatively ($p < 0.001$) and for primary versus secondary ones ($p < 0.01$). The total dose was a marginally significant factor for local control [57].

Alaniz-Camino, after treatment of 483 pterygia with postoperative β-irradiation at a dose of 28 Gy in 4 to 5 days overall time starting 24 h after surgery, reported a 4.32% recurrence rate with no undesirable morbidities [3].

Fukushima et al. in their study on 393 pterygia reported a recurrence rate at 8.6% and 71% of them were noted within 1.5 years after treatment (Table 1). Local control was significantly lower in females ($p = 0.05$), previously treated cases ($p = 0.007$), with long overall treatment time, 35 days versus more ($p = 0.01$), and those

Table 2
Willner study on treatment with soft X-ray therapy.

Author	Lesions	Treatment schedule	Type of irradiation	Follow up	Rate of local control	Late effects
Willner et al. [78]	81 recurrent pterygia	Excision + radiotherapy (4 fractions of 5 Gy after a mean of 4 days from surgery: 42% (1st group). 7 Gy + microsurgery + conjunctival graft + 5 Gy to surgical bed within 24 h then every other day to 27 Gy: 58% (2nd group).	RT50 (Philips) with a 20 kV X-ray generator and 0.1 mm aluminum filter with special tubes (source–surface distance: 40 mm and diameter: 10–15 mm)	Median period 57 months (1st group) Median period 26 months (2nd group)	Actuarial 2 and 5 years freedom from recurrence rate: 66% and 44% in 1st group, and 91% in the 2nd group ($p = 0.001$). Recurrences: 1st group: 15/34, 2nd group: 4/47	No serious side effects e.g scleral necrosis, thinning, no cataract, no glaucoma

younger than 30 years ($p = 0.001$). The time interval between excision and start of irradiation did not affect the outcome nor did the total dose (30 Gy versus 35 Gy). Visual disturbance, pain, congestion and ulcerations appeared in 5.3%, 3.3%, 2.5%and 0.5%, respectively [27].

Wilder et al. in a study included 338 pterygia reported a recurrence rate at 9.8% (Table 1). Better local control appeared in those received three weekly 8 Gy fractions and a single fraction of 18 Gy versus those received a single fraction at 8–10 Gy or two weekly fractions of 8 Gy, when irradiation initiated 1–8 h postoperatively and in primary pterygia. Ocular irritation, decreased visual acuit, and photophobia developed in 17, 11 and six cases, respectively [77].

Wesberry et al. reported on 171 pterygia received a single postoperative dose at 20 Gy (Table 1). Recurrences affected 8% of cases and only 3% presented minor side effects [76].

Beyer in his study on 146 lesions found that all recurrences (13 cases) developed within the first 18 months after treatment (Table 1). The time between surgery and irradiation, age, bilaterality and prior resections were not correlated with recurrence rates. Transient conjunctivitis and photophobia were frequently noted [11].

Monteiro-Grillo et al. after follow up of 100 lesions treated with excision and postoperative β-irradiation reported a recurrence rate at 14%, with a median time of recurrence at 11 month (Table 1). Better local control was achieved in primary pterygia. Early toxicities including ocular irritation, neovascularisation and limited scleral atrophy developed infrequently and recurrent lesions experienced greater incidence of sequelae. No significant correlations were found between treatment sequelae and radiation doses ($p = 0.32$) [53].

Schultze et al. analyzed the results of 64 primary and recurrent pterygia treated by postoperative β-irradiation at a total dose of 30 Gy/six fractions/2 weeks. With a median follow up period of 5.5 years, 8.16% of primary and 26.7% of recurrent lesions recurred. Irradiation initiated within 3 days postoperatively achieved better control in primary cases [66].

Campbell et al. reported an 89% local control rate after resection and postoperative β-irradiation of 48 recurrent pterygia. Irradiation initiated immediately postoperatively at an average dose of 50 Gy. After a median follow up period of 14 months, no serious complications nor cataract were noticed [14].

4.3. Contact X-ray irradiation as an alternative therapy to β-irradiation

In 1970, Papillon et al. published the results of using Philips contact therapy treatment unit with a 50 kV X-ray generator in treatment of squamous cell carcinoma of the sclero-corneal limbus. The problem of local control was similar to the pterygium situation. And good results were achieved with doses of 50–60 Gy/five fractions/6 weeks [61].

In view of the discrepancies reported by some authors between the dose rates measured at the 90Sr applicators surfaces and those quoted by the manufacturers which may reach up to 32–35% and because of the possibility of imprecision in dose delivery to the surgical scar due to the circular motion of the 90Sr applicators on the conjunctiva that may be needed to cover the whole surgical scar, Willner et al. published in 2001 their results in using soft X-ray therapy instead of β-irradiation in treatment of recurrent pterygia [28,67]. They adopted a new treatment policy included preoperative single dose of X-ray that enabled the therapist to determine exactly the preoperative extension of the lesion and the subsequent adjustment of the treated area. This was followed immediately with surgical optimization using microsurgical excision and conjunctival autografting then postoperative radiotherapy starting early after surgery. They compared the results of this new policy with their older one composing of surgical excision of the recurrent pterygia by bare sclera technique and postoperative radiotherapy (details in Table 2). The resulting depth dose conformed fairly to depth dose of 90Sr eye applicators. All dose prescriptions were surface doses. Following local anesthesia, eyelid clamp was positioned and an adequate tube carefully positioned to cover the surgical bed. Nineteen recurrences were noted, 76% of them within the first 2 years. Treatment with pre- and postoperative radiotherapy was significantly associated with a better local control. No severe side effects like scleral necrosis, thinning, iris atrophy, glaucoma or cataract developed [78].

5. Discussion

The high recurrence rates after simple excision of pterygium is the most frequently encountered problem [21,35]. It ranges from 20–39 to 30–50% and in some studies up to 89% [10,11,15,18,32,33,35,56,62,73]. Postoperative β-irradiation has been one of the traditional adjuvant therapies used for reducing these recurrence rates since 1950 [15,25,27,29,57,62,74]. The ESTRO Nice conference on radiotherapy for non-malignant diseases has considered the use of radiotherapy as an accepted indication (A category) in the treatment of pterygium especially in recurrent and more complicated cases [44]. Unfortunately, studies concerning this issue are often retrospective enrolling variable numbers of patients from different origins treated by surgeons with different experiences and various postoperative irradiation doses and schedules that started at variable postoperative time intervals and followed up for different periods. Such factors could be responsible

for the variety in local control rates that ranged from 70 to 98.5% [55,62].

Radiation doses reported in these studies ranged from a single large dose at 20–30 Gy [11,35,76] to 60 Gy/six fractions/6 weeks, however, doses of 30–35 Gy/three fractions/2–3 weeks were frequently used schedules and associated with recurrence rates up to 11.8% [21,27,33,53,55,57,62,75]. The use of a single radiation dose is reported here in three studies using doses from 20 to 30 Gy [11,35,76]. No or very low incidence of severe side effects were reported and good local control was achievable with rates of recurrence varied between 6.8 and 9.4%, but in view of the follow up periods of these studies, the higher rates of late side effects reported in other long term follow up studies and referring to the radiobiological work of Brenner et al. who estimated a large α/β value for disease control (25 ± 9 Gy), it is useful to design a multifractioned treatment that would be expected to give comparable control rates to a single fractioned treatment with less expected late complications [10,11,12,35,47].

Time between surgery and start of irradiation appears crucial in many studies, lower rates of recurrence were reported when irradiation initiated within 24 h after surgery and within 3 days versus more than 3 days postoperatively [21,35,55,57,62,66,75,77]. However, other investigators did not report such an observation [11,27,33]. Among the factors correlated with higher recurrence rates was the type of pterygia. It was evident from our review that recurrent pterygia are associated with higher rates of recurrence compared with primary ones [21,33,53,62,75,77,78]. This may be explained by the presence of higher levels of cellular proliferation in the subepithelial fibrovascular layer of pterygium compared to normal conjunctiva as shown by flow cytometry measurements and the observation that the proliferation rate of fibrovascular tissue from recurrent pterygia was additional 10-folds increased compared to primary pterygia [70,78]. Severe side-effects such as scleral ulcerations, scleromalacia, necrosis as well as radiation induced cataract were reported in most studies at a very low or no incidence in contrast to a rate at 4.5% for severe scleral thinning reported by others [74].

β-irradiation is believed to cause endarteritis obliterans, but it is unlikely to be the only factor responsible for such rates of complications as bare sclera excision itself can cause surgically induced necrotizing scleritis years after surgery without the use of adjuvant treatment [5]. In view of the few number of studies addressing contact X-ray therapy as an alternative to β-irradiation and referring to the rates of local control and safety reported, further comparative studies between these two modalities are warranted.

6. Conclusions

In spite of the paucity of randomized controlled studies on postoperative β-irradiation in the treatment of pterygium and the heterogeneity characterizing the retrospective studies, we can conclude, based on the aforementioned results, that β-irradiation using 90Sr applicator appears effective in reducing the rates of recurrence after surgical resection of pterygium, especially the primary ones, and safe even in the long-term. It will remain one of the standard adjuvant therapies after surgical excision of pterygia for its convenience and simplicity. Although a considerable debate exists concerning the total dose and fractionation regimen, it appears from clinical evidences and referring to the radiobiological studies that a fractionated dose of 30 Gy in three fractions over 2–3 weeks starting within 3 days from surgical excision could achieve local control as good as that associated with higher doses with less expected late side-effects. Application of a single dose of β-irradiation and the use of contact X-ray therapy instead of β-irradiation needs to be compared with fractionated β-irradiation in long-term controlled randomized studies.

Conflicts of interest

None.

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